

## **REMARKS**

Claims 21-22 are pending in the application. No claim is allowed.

Claims 21-22 are rejected under 35 USC 103(a) as allegedly being unpatentable over Brekke, et al. (WO 94/09722, "Brekke"). Applicants respectfully traverse the rejection and request that it be reconsidered and withdrawn.

The Examiner relies upon Brekke to show compositions for treatment of bone. It is submitted that upon a careful reading of Brekke, several elements are required in order to induce bone formation. First, one must have structural competence, that is, a gross structure to provide a mechanical support and structural surface for the dynamic biological processes for genesis, growth and development of new non-calcified and calcified connective tissue. This function is served by the biologically acceptable, biodegradable solid polymer (such as polylactic acid) arranged as a one piece porous solid body with enclosed randomly sized, randomly positioned and randomly shaped interconnecting voids, each void communicating with all of the others, and communicating with substantially the entire exterior of the body. Next there must be a microstructure composed of the solid chemotactic ground substance, which can be hyaluronic acid. The hyaluronic acid is used as a solid material, a velour composed of fibrils with intercalated voids of microscopic dimensions. Thirdly, Brekke requires the osteoinductive/osteogenic substance which is a growth factor. These requirements dictate the use of a solid composition as shown in Brekke's FIGS. 1-6, and described on page 20, lines 18-26.

However, the presently claimed method requires the application of an injectable liquid composition onto a tissue site of desired bone growth. See Specification, page 3, lines 18-25. The useful injectable composition is advantageous because it need not be molded into a solid that precisely fits the space in the bone. See Brekke, p. 24, lines 29-34.

The examiner points out that hyaluronic acid as a gel may be injected into the solid porous polylactic acid block. Brekke, page 20, lines 11-13. But the block is not a tissue site. Also, the injectable composition, containing only HA and perhaps a diluent, does not contain all the necessary

components of the injectable composition recited in the present claims. Furthermore, in Brekke, the HA is then lyophilized *in situ* to convert it to the ground chemotactic substance of Brekke's invention. Thus, as applied for use, it is not injectable.

The examiner also points out that the growth factor is an injectable composition and that it is injected into the polylactic acid block. Brekke, page 19, line 30 ff. However, as an injectable composition it also lacks all of the necessary components of the injectable composition recited in the present claims.

The fact that two of the components, HA and the growth factor, can exist separately as injectable compositions prior to their use does not lead one to combine both of them onto an injectable composition to a tissue site of desired bone growth. Brekke directs one not to do that. Brekke deems it necessary to use the polylactic acid block for reasons set forth, for example, on page 4, lines 11-19. In particular, Brekke requires the polylactic acid block to:

“(function) as a carrier for other constituents of the invention which do not have mechanical and structural competence.” (Page 4, lines 17-19.)

These “other components” include the HA and growth factor.

In contrast, according to the present invention, the recited components are injected as a liquid together onto the tissue site of desired bone growth. See p. 4, lines 8-17; p. 3, lines 18-25; p. 5, lines 21-23; p. 11, lines 2-11 and 18-21; p. 13, lines 18-21; and p. 19, lines 14-19.

Therefore it is submitted that the teaching of the methods in Brekke to one of ordinary skill in the art would be that in order to induce the growth of bone, one needs the solid macrostructure, and possibly also the solid microstructure, of the device in Brekke. This is a teaching away from the presently claimed method applying an injectable liquid composition containing all of the recited components onto a tissue site of desired bone growth.

For the foregoing reasons it is submitted that the claims are unobvious under 35 103(a) over Brekke. Entry of this amendment and withdrawal of the rejection are respectfully requested.

Respectfully submitted,  
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